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*Case Report*

# Hurry Up! If not treated, Mucormycosis is lethal

Mucormycosis

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**Abstract**

Mucormycosis is a rare fungal infection with high morbidity and mortality in immunosuppressed patients. It is frequently associated with immunosuppressive conditions such as diabetes mellitus, hematologic malignancy, high-dose chemotherapy, AIDS, and transplantation patients. A necrotic lesion on the edge of the nose was developed in the intensive care unit of the patient with myelodysplastic syndrome (MDS) seconder acute myeloid leukemia (AML). Mucormycosis was diagnosed with physical examinations and histopathologic findings. Although the patient was given an antifungal therapy, he died. This case was reported to emphasize the mucormycosis which results in high mortality.

**Keywords**

Mucormycosis; Mortality; Hematologic Malignancy

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## Introduction

Mucormycosis is a rare fungal infection with high morbidity and mortality in immunosuppressed patients. *Mucor* is a mold fungus belongs to *Mucorales* team of the *Zygomycetes* class and causes an invasive fungal infection. Mucormycosis is classified according to organ involvement. Rhinocerebral involvement is the most common clinical form. Pulmonary, cutaneous, gastrointestinal, and disseminated mucormycosis are the other forms. In diabetic patients rhinocerebral mucormycosis, in patients with neutropenia due to bone marrow transplantation and leukemia rhinocerebral and pulmonary mucormycosis, in malnourished patients gastrointestinal mucormycosis are more common. Mucormycosis is caused by the inhalation of mold fungi commonly found in nature. While spores of mucormycosis are destroyed by phagocytes in healthy subjects, spores may cause infection with invasive vascular endothelium in cases with immunosuppression or phagocytic dysfunction [1,2].

The current study, aimed to present a patient with rhinocerebral mucormycosis with acute myeloid leukemia (AML) which was secondary to myelodysplastic syndrome (MDS).

## Case Report

A 77-year-old male patient with AML secondary to MDS was treated with azacitidine chemotherapy. He was admitted to the hematology clinic for respiratory distress after chemotherapy. There were rales at right lung middle lobe on physical examination. Initial laboratory investigations showed that the number of white blood cells (WBC) was 5620 $10^6$ / L, hemoglobin (Hb) was 11,9 g / dL, platelet count (TS) was 100 K / uL, C-reactive protein (CRP) 17 mg / dL (normal range: 0-5 mg / dL), procalcitonin was 36,4 ng / dL (normal range: 0-0.1 ng / dL). 25% of the polymorphonuclear leukocytes (PMNL) and 52% of the lymphocytes were observed in the peripheral blood smear. Intravenous (IV) therapy with piperacillin / tazobactam 3 x 4.5 mg was started with pneumonitis due to infiltration of the right middle-lower lobe on chest x-ray. Treatment with vancomycin 2 x 1 g IV antibiotherapy was added at 48 hours of treatment with the cause of the patient having 38.4 ° C fever and decreased WBC (3920 $10^6$ / L; PMNL: 6%) and CRP: 184 mg / dL. For neurotropic development, the dose of piperacillin / tazobactam was changed to 4x4.5 mg. Under current antibiotherapy, progression in pneumonic infiltration, fall in $O_2$ saturation and elevation of fever were observed. Consequently, the patient was considered an invasive fungal infection and voriconazole 2x4 mg / kg treatment was begun (loading dose of voriconazole 2x6 mg / kg). The patient with immunosuppression was also evaluated for tuberculosis. There was no history of tuberculosis in the family; the patient had one BCG scar. Quantiferon test and acid-fast bacilli (AFB) test (three times) were negative. Improvement in the patient's clinic and laboratory parameters along with the radiologically significant regression in the lung infiltration were detected. The patient was discharged at his own request by signing while current treatments continued. The patient was discharged with moxifloxacin 1 x 400 mg tablet and voriconazole 2 x 200 mg tablets.

On the 7th day of discharge, the patient was admitted to the intensive care unit with a complaint of shortness of breath. On physical examination, the general condition was moderate, conscious and cooperative. Fever: 37 °C, pulse: 120 beats / min, arterial blood pressure: 100/60 mmHg, respiratory rate: 20 / min. In pulmonary auscultation, there were crepitant rales in bilateral lower zones. Other system examinations were normal. In laboratory tests WBC: 710 $10^6$ / L (PMNL 24%), CRP 89 mg / dL. Piperacillin / tazobactam 4x2.25 g IV (creatinine clearance 32 mL/min) and voriconazole 2 x 200 mg tablets were restarted to patient. On the third day of admission, vancomycin 1x1 gr (48h) was added to current treatment due to high fever (38.1°C) and CRP value (144 mg / dL). Under these treatments, black and necrotic lesion appeared around the nose (Figure 1A). Considering mucormycosis in the patient, liposomal amphotericin B 5mg / kg / day treatment was started. An emergency biopsy was performed by the otolaryngologist. Furthermore, maxillofacial computed tomography (CT) was performed (Figure 1B). Microbiological and histopathological samples were taken. Debridement could not be performed because the general condition of the patient was not favorable. Inflammatory necrotic sinus fragments containing pathologic fungal microorganisms were reported as mucormycosis (Figure 1C, 1D). The patient died on the 5th day of liposomal amphotericin B treatment.

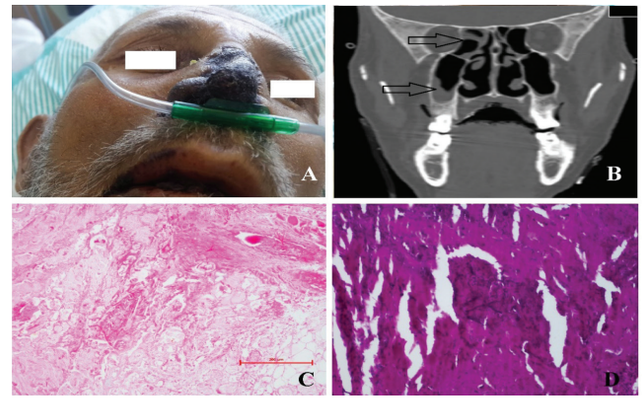


Figure 1. A: Necrotic area in the nose of a patient. B: Mucormycosis in the right maxillary and ethmoid sinuses in maksilofasial BT. C: Hematoxylin and Eosin (H&E) staining was performed at 20x magnification, hyphas were irregular and were seperated from main hyphae by 90 degree angle. D: PAS, hyphas were dyed basophilic.

## Discussion

Mucormycosis colonizes in immunosuppressive, hematologically malignant patients and diabetics. Impairment of the phagocytosis mechanism leads to necrotizing infections that involve severe invasive granulomatous progressive vessels and tissues [3]. The most common predisposing condition is DM (60-80%). Other immunosuppressive conditions such as hematologic diseases, malignancy, chronic renal failure, antineoplastic agents, immunosuppressive treatment, usage of corticosteroid, protein-calorie malnutrition, organ and bone marrow transplantation and AIDS are also included in the etiology [4]. The most frequent predisposing factor in the study by Yohai et al. was DM (60%) [5]. Similarly, in the study by Ferry et al. DM was found to be leading predisposing factor with 83% [6]. In another study, hematologic pathologies were detected as predisposing factors in 32 of 79 cases [7]. Mucormycosis is most frequently seen in acute leukemia among hematological malignancies. In the study by Pagano et al. this rate was reported as 78% [8].

In our case, the patient had hematological malignancy and neutropenia. The lesion was the necrotic tissue of 1.5x2 mm in the

lateral aspect of the nose right wing at first, and the tissue defect covered the large part of the nose within 48 hours. The treatment of mucormycosis infection should begin as soon as possible because mortality rate of the disease is high. A definite diagnosis is made by showing characteristic hyphae in materials such as disease, tissue, sputum or exudate. For diagnosis, tissue samples must be obtained with invasive techniques such as biopsy or surgery. Premortal diagnosis of mucormycosis infections is very difficult. It has been reported as 35% in a retrospective study [8]. Without the pathologic diagnosis of the disease, it was thought that the present lesions could have mucormycosis in appearance. Therefore, liposomal amphotericin B 5mg / kg / day was started to the patient immediately. Although liposomal amphotericin B therapy was initiated, the patient died within 5 days.

As a result, mucormycosis infections should be kept in mind in immunosuppressed cases with necrotic skin lesions.

*Scientific Responsibility Statement*

***The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.***

*Animal and human rights statement*

***All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.***

*Conflict of interest*

***None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.***

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